Methods of Stopping or Reversing Early Carious Lesions

Fluoride: A European Perspective

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Abstract:

The purpose of this review was to discuss the findings of the systematic review on the management of the early carious lesion with fluoride from a European perspective. The review was checked and the overall finding that the evidence was incomplete was confirmed. It was suggested that the reason that few data were available was that clinical trials had not been designed to answer this question and that the baseline of healthy surfaces and surfaces with very early lesions were rarely quantified. The European perspective would want to identify a clinical method that could manage these lesions better than the home use of fluoride toothpaste. Future research was recommended in the form of several systematic reviews and re-analysis of existing data. Only then could further studies be recommended. In modern European dentistry restoring these lesions is not an option

Keywords: non-cavitated carious lesion, fluoride, Europe

The diversity of Europe is such that it is not possible to present one point of view as the European Perspective. The use of fluoride across Europe ranges from the Irish emphasis on water fluoridation with legislation in its favour through the French and Swiss using salt fluoridation to the major use of professionally applied fluorides on an individual basis in Scandinavia. Not only is the use of fluoride diverse throughout Europe but so is the practice of dentistry. The difference in the delivery of services varies from emphasis on the independent practitioner to those employed within salaried services. Within Europe there also is a wide variation in the importance given to a population approach to the prevention of disease. In essence then the discussion I give you has to be influenced by my European background, which is that of a British practitioner of dental public health with considerable experience of undertaking systematic reviews.

My objectives in this presentation are:

- To identify if any studies have been missed from the RTI/UNC review
- To discuss limitations identified
- To make recommendations for future research

The review undertaken for this conference is an impressive piece of work. The difficulty of systematic reviews should not be underestimated nor should the problems of interpretation when little reliable evidence is found. In this case the major finding of the review regarding the ability of fluoride to stop or reverse initial carious lesions is *'incomplete.'* Can this really be true? Surely, incredible amounts of research have been undertaken on the effects of fluorides at an individual level on initial dental caries?

My first task was to identify any studies that were missing from this review. I undertook this task in the following way:

- I repeated the searches undertaken by the review group but I used slightly different key words. I added the word 'prevention'. The purpose of altering the key words while keeping the searches broad was to try to see if any studies were omitted by the use of the group's key words.
- I, too, limited my search to Medline and excluded languages other than English and the grey literature.
- I, then, scanned the abstracts against the inclusion criteria and, for those that appeared to meet the inclusion criteria, read the papers.

It is important to note that, unlike the RTI/UNC report, these processes were not double-checked.

Having completed this process I can report that I found two additional papers that, in my opinion, fulfil the inclusion criteria. I have extracted these papers that are presented as an additional evidence table (Table 1).

These papers report two studies. The first compared a 0.2 percent sodium fluoride rinse with a difluorosilane varnish using radiographs on the approximal surfaces of molar and premolar teeth.[1] The progression of initial lesions was slightly less in the varnish group but statistical tests were not reported for this analysis.

The second paper reported a comparison of 0.2 percent sodium fluoride with 0.025 percent sodium fluoride both used as a weekly rinse.[2] The author reported the surprising conclusion that the 0.025 percent solution was more effective at preventing caries than the 0.2 percent solution. However, when only looking at the effect on initial lesions the picture was confusing; more initial lesions progressed with the

lower concentration but more lesions also regressed with this solution. Again statistical tests were not reported for this analysis.

These two additional studies do not add much to those reported in the RTI/UNC report. The total number of studies identified only increases from five to seven and there remains the very varied nature of study design and population characteristics with which to contend.

I, therefore, agree with the conclusions already presented about the quantity and quality of the evidence base for the questions asked. As I have described, in coming to this conclusion, it was necessary for me to read some of the papers identified in my search to see if they met inclusion criteria. As I read, I was able to find some of the reasons why the quantity of evidence was so little. I plan to highlight some of these papers to illustrate points I wish to make but it is important to stress that in doing this I am breaking the principles of systematic reviewing and may be introducing my bias to the discussion. I plan to cover this problem when I return to discussing future plans for research.

At the same time many questions were raised in my mind. The first and most obvious question is where do we go from here? It is at this point that my European public health perspective enters and asks a fundamental question. Were the most appropriate questions posed in this review? I believe that if this had been done in Europe the questions would have been asked in a different way. It is important to stress that neither approach is correct. They are just different.

Looking back at the research and reading the papers it is quite clear that considerable amounts of research have been undertaken. That is clearly stated in this review that started by looking at 1435 citations. So why did the inclusion criteria

exclude them? I would suggest that one reason is a conflict in the outcome measures used in previous research and the outcome measure searched for in this review.

What do I mean about this conflict with outcome measures? As the review states, 'Most forms of non-cavitated lesions have been excluded from the examination used in clinical trials.' In other words in clinical trials the measurement was from no caries to caries that required operative intervention or from initial caries to caries that required intervention. What is generally not done is to measure lesions that stop or lesions that reverse and to report them (Figure 1). Clearly, this is of prime importance in studies concerning fluoride given the current understanding of how fluoride works. This leads to two problems. The first is that in existing studies there is not a baseline measurement exclusively either for healthy tissue or for initial caries so it is not possible to determine the point from which you are starting.

The second problem has been reviewed in detail in the first part of this conference and that is the ability to measure initial dental caries. Only if this can be done accurately in a clinical setting is it possible to evaluate accurately the effect of any clinical intervention on initial lesions.

My second major question in the design of the review is regarding the decision to exclude studies where fluoridated toothpaste was used in either the experimental or control arm. From a European perspective, fluoride toothpaste is seen as the major plank in the control of caries both at an individual level and in the public health approach. I would only be interested in recommending a clinical method that produced better results than the use of fluoridated toothpaste by an individual. I would also suggest that there are sound ethical reasons for taking this approach.

I have problems also with the emphasis on professional application of fluoride materials. I agree that this is a very useful method of assessing such items as fissure sealant but surely given our current knowledge on the mode of action of fluoride - little and often - the assessment of self-applied fluoride would be of far more benefit. From a European perspective, with the exception of Scandinavia, it is not possible to envisage a situation where professionally applied fluorides would be available on a very frequent basis except to specific high-risk groups.

We may be lacking evidence in exactly which fluorides to use to halt or reverse initial lesions but I do not consider that this should then result in restoring these lesions. The evidence from a systematic review of restoration longevity does not allow us to identify what factors will ensure longevity or how to achieve clinical trial results in everyday practice.[3, 4]

Where do I think that the research in this area should go? There are three major tasks that I believe should be undertaken as a matter of some urgency.

The first is to identify suitable study designs for answering this question. It is necessary that this should be specified in some detail including the study populations to be used, the data that need to be recorded and the confounding variables that should be considered.

I entirely support one of the recommendations of the report. Where possible, radiographic studies need to be re-analysed using the criteria decided in the earlier part of this consensus conference. There are, of course, methodological problems in doing this. In particular it is important to decide whether the study design allows for the new question to be answered. Consideration needs to be given to the secondary

analysis of data. Are the analyses appropriate? Is the population the correct one for the analysis now being undertaken?

The third piece of research that is needed is to prepare three further systematic reviews. These should pose slightly different questions and use different inclusion criteria. I am not suggesting that this review be repeated, but rather, that it should be extended, by looking at slightly different topics. The first extra review would look at caries preventive methods using *in situ* methodology. While this is an unusual suggestion for a systematic review I would suggest that it would be of benefit here as a way of suggesting which techniques might be the most promising to then test in a clinical setting.

The second review would be to look at the effects of fluoridated toothpastes on caries in general and on initial caries in particular and the third review would be to look at topical fluorides on caries in general. These last two reviews have protocols registered on the Cochrane data base along with five other reviews on similar areas.[5-11] These reviews should give useful information but until they are published it will be impossible to see how much more data is added to the question of particular interest to this audience – 'What is the effect of fluoride on initial caries?' There is also a meta-analysis on the subject of topical fluorides that provides valuable data.[12] It highlights the problems caused by the great heterogeneity between studies and this is something that needs to be considered in future research. It is interesting to note that these same problems were found in the systematic review of water fluoridation of public water supplies – major heterogeneity between studies.[13, 14]

Once these tasks are finished it will then be possible to commission appropriate research designed to fill in the holes identified by the systematic reviews. These would fulfil the criteria identified in my first proposed piece of research. By planning

the research in this way it would be possible to reduce greatly the heterogeneity between studies and allow studies to be combined. Of course, the disadvantage of approaching it this way would be that it would limit the generalizability to the whole population. However, this would be preferable to the current situation where we neither know what works or whether it is applicable to any part of the population.

From a European perspective, there is a major need to progress this work; the diagnosis and treatment of early carious lesions. To restore these is not an option in the practice of modern European dentistry.

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Table 1. Additional papers identified for RTI/UNC Evidence Table 3

	Author, Year	Type of Design	Duration	Country and F Status	Experimental agent	Frequency	Comparison agent	Subj. Age	N of Subj. in analysis
1	Brunn, Bille, Hansen et al, 1985	Non-RCT (double blind)	36 mo	Sweden NR	Difluorosilane varnish	Twice a year	0.2% NaF solution 10mls every 2 weeks	9 to 12 yrs	251
2	Forsman (1974)	RCT (double blind)	24 mo	Sweden <0.2 ppm	NaF 0.025% solution 10 mls	Weekly	NaF 0.2% solution 10 mls weekly	11 to 12 yr	270

	Tooth Type	Surface	Exp. Lesion N	Com. Lesion N	Criteria for Non-Cavitated Lesion at Baseline	Criteria for Progression	Criteria for Reversal
1	Molar and premolars	Approximal surfaces	50	75	Radiographic changes in enamel that have not reached ADJ	Must have reached ADJ	NR

2	Molars and premolars	Approximal surfaces	91	109	Radiographic changes in enamel only	Lesion into dentine	No radiographic evidence of lesion

	No. of Examiners	Inter-Examiner Reliability	Mean Intra-Examiner Reliability	Type of Analysis	Compliance Estimate	Attrition from Baseline
1	1	NR	NR	All at final examination	NR	30%
2	1 (with confimation when necessary)	NR	NR	All at final examination	NR	6%

	Percent of Lesions progressing		Percent of Lesions Reversing		Quality Score		
	Exp.	Com.	P-value	Exp.	Com.	P-value	
1	50%	44%	NR	NR	NR	NR	65
2	30%	23%	NR	9%	3%	NR	65

Figure 1. Caries Measurement